

Supplemental Tables

Table S1 Mutagenic primers (all 5'→3'). Mutant nucleotides are in bold font; corresponding codons are underlined.

Human Txnip P135L	Fwd	ACCGCCGAGCCAG <u>CT</u> AACTCAAGAGACAAA
	Rev	TTTGTCTCTTGAG <u>TTA</u> GCTGGCTCGGGCGGT
Human Txnip H241S	Fwd	GTCATCAGTCAGAGGA <u>ATAG</u> TATTATCTCAGGGACATGC
	Rev	GCATGCCCTGAGATA <u>ATAC</u> TTCAGCTCTGACTGATGAC
Human Txnip P347A	Fwd	ATCACCGATTGGAGAG <u>GC</u> AAACC <u>ACT</u> CCTCTGCT
	Rev	AGCAGAGGAGTGG <u>TG</u> GCCTCTCCAATCGGTGAT
Human Txnip Y221F	Fwd	ATTGTGGCCGCCACACT <u>TC</u> CTGCCAATGGCCAGAC
	Rev	GTCTGCCATTGGCAAG <u>GA</u> AGTGTGGCAGGCCACAAT
Human Txnip K286S	Fwd	AGCGTTCTGGAT <u>CC</u> <u>AGT</u> AAGTCATCCTGAC
	Rev	GTCAAGGATGAC <u>CTT</u> <u>ACT</u> GGATCCAGGAACGCT
Human Txnip C247S	Fwd	CATATTATCTCAGGGACA <u>AGC</u> GCATCATGGCGTGGC
	Rev	GCCACGCCATGAT <u>CGC</u> <u>T</u> TGTCCTGAGATAATATG
Mouse Arrdc4 C184S	Fwd	GAGAAAATGGTGG <u>C</u> <u>AGT</u> GGCTTTCACCTC
	Rev	GAGGTGAAAAG <u>CCA</u> <u>ACT</u> GCCAACCATTTCTC

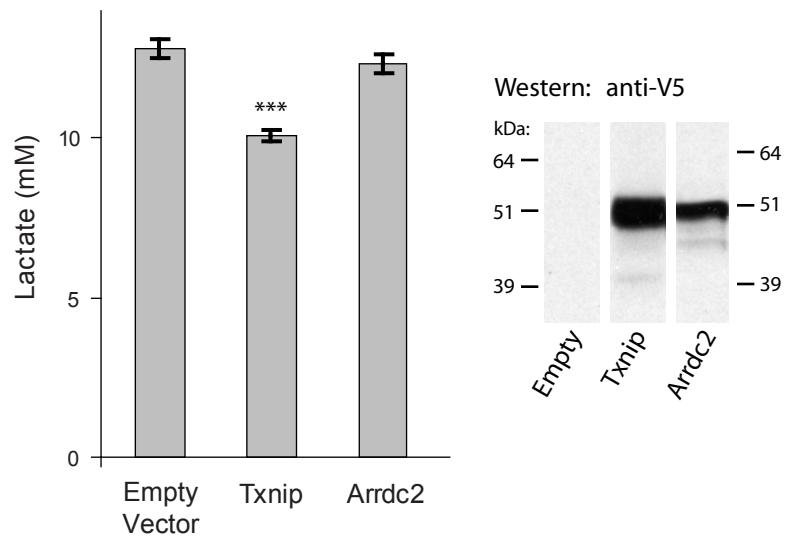
Table S2 Overlapping primers for making Txnip-Arrdc3 domain-swap chimeras (all 5'→3').

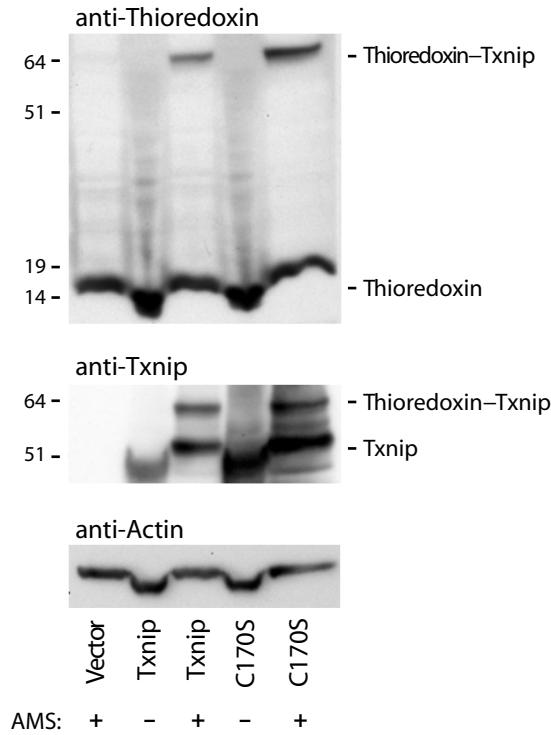
Arrdc3 N-Arrestin to Txnip C-Arrestin	Fwd	ccatctctacatccat tttagcagcagaacatccagcatggc
	Rev	tagcagacacagg tgc <u>c</u> agtaatgaaggagtgtga
Txnip N-Arrestin to Arrdc3 C-Arrestin	Fwd	gtcaataccc tgatttaatgt <u>c</u> accccaaggcaggcaca
	Rev	tgtgcetctgggtg acattaaatcagggatttgcac
Arrdc3 C-Arrestin to Txnip C-Tail	Fwd	ccatctctacatccat tttagcagcagaacatccagcatggc
	Rev	ggccatgtggatgtctgtct aaatggatgttagaggaatgg
Txnip C-Arrestin to Arrdc3 C-Tail	Fwd	attggcagcagatcagg tcttaggttagcagaacctcaagtgt
	Rev	tacacttgagg ttctgtcac <u>t</u> tagac <u>c</u> ctgtcgccaa

Supplemental Figure Legends

Figure S1 Effect of Arrdc2 on lactate output. 293T cells were transfected with pcDNA 3.1 empty vector, mouse Txnip-V5, or mouse Arrdc2-V5. Conditioned medium was assayed for lactate concentration. Overexpression of Txnip significantly inhibited lactate output while Arrdc2 had no significant effect ($n=5$, *** $p<0.001$ vs empty vector). Western analysis with an anti-V5 antibody demonstrated expression of both Txnip-V5 and Arrdc2-V5 (discontinuous lanes from a single gel are shown).

Figure S2 A) 293T cells were transfected with wildtype Txnip and Txnip C170S. Western analysis of AMS-alkylated lysates detects a Txnip-thioredoxin for both wildtype and C170S Txnip. B) Alignment of *C. elegans* (worm) and *Drosophila melanogaster* (fly) alpha-arrestin sequences homologous to the sequence surrounding human Txnip Cys-170. C) 293T cells were transfected with empty pcDNA3.1, human Txnip, human Txnip C170S, empty pcDNA4/HisMax, mouse Arrdc4-Xpress, and mouse Arrdc4-C184S-Xpress. Txnip significantly inhibited lactate output while Txnip C170S had no effect compared to empty pcDNA3.1. In contrast, Arrdc4 and Arrdc4 C184S both significantly inhibited lactate output from 293T cells compared to empty pcDNA4. $n=4-5$, * $p<0.05$, *** $p<0.001$.



A**B**

Human Txnip	DVN--TPDLMAPVSAKKVSCMFIPDGRVSVSARIDRKGFCEGDEI	195
Human Arrdc3	DIN--TPSLLSPQAGTKEKTLCCWFCTSGPISLSAKIERGYTPGESI	208
fly CG18746	DLNSESMLRVPSPQVESQRTFCCFPCCRSSPLSMRLSVPQSGFVPGQIV	195
fly CR18748-B	DINTYNVSQVPVQAKTEKTFGVWPFRSDPLTLELNLPQTGFVPGQTV	146
fly CG18745	DLNFDSPLLVRPAHSETSKTYCCWPCRSDPLALQLTVQPTGFVPGQNV	195
fly CG18747	DLNFDTDPQLKSAAHSEGYRTFCCGPCKTDPKLLELHLHQAGYVPGQKI	197
fly CG10086	DLNQETKMLREPASNEAVEHFCCLMHTK--PVQLKVTLQQQGYVPGQFM	200
worm F35F10.12	DLN-VIPHALTQINDQASENLGCCCFTKGYLELRVNIPKTGFVPGETV	203
worm T20D4.6	DLN-VIPHSLTPINTQASENLGCCCFKNGFLEMNVNIPKTGFVPGETV	203
worm Y17G7B.11	DLN-ITPTAINPMVNTASKNTG-LILKKGLVTITVNLPKRGYVAGEIM	199
worm ZK938.4	DLR-LIPNSQVPSKKHVCEFGAVLWKNGLVRMELRLPKQGFVCGENI	203
fly CG1105	DLN-LNPRVKEPFKLELEKSFCFCRSGPLAVITNIPQTGFVSGQVL	199
worm Y49E10.24	DLN-KEVLASEETSSWKSKKVGFLLFRYGVNLQIRIPKKGYVPGETI	207
fly CG2641	NLN-MSPQLLMPLVREDIKHFCCWPCSSGPVLSTLTIPFGGYAPGQKI	192
worm T12D8.4	DINSDPKLNEPATCVESNHAVTFCCRSAGSVTGEIRISKCGYTPGEKI	199
fly CG7047-B	DLNLEKPILAQPFTCEVEHKLGIVCVGGGQIKCRVSLDRGGYVPGENI	190
worm F40F8.8	D--SMEEKYLSPLSAQDRKVNCC#CCORGALALRIILERTAYVCGENI	193
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